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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,980	01/14/2002	Stephen Michael Cohen	71745/55880	7236

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EXAMINER
CARLSON, KAREN C

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,980	COHEN ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *17-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2 IDSs* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election without traverse of Invention I, Claims 1-16 is acknowledged. Claims 17-25 are being withdrawn from further consideration by the Examiner because these Claims are drawn to non-elected inventions.

It is noted that the instant application is a 371 of PCT/IB99/01891, filed November 3, 1999 and claiming priority to foreign application GB 9824045, filed November 3, 1998. However, SEQ ID NO: 1 is not found in the PCT; the sequence disclosed in the PCT lacks two lysines at amino acid residues 67 and 68. Therefore, until this new matter issue is resolved, SEQ ID NO: 1 an dfunctional equivalents to SEQ ID NO: 1 will receive priority only to the filing of the instant application, January 14, 2002.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The protein claimed is not indicated to be purified or isolated and therefore reads on a protein found in nature.

Claims 15 an d 16 provide for the use of a protein or fragment of a protein comprising SEQ ID NO: 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 15 and 16 are is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As noted above, SEQ ID NO: 1 is not found in the PCT; the sequence disclosed in the PCT lacks two lysines at amino acid residues 67 and 68. Thus, this is new matter added to the national stage application.

The specification does not provide a written description of functional equivalents of SEQ ID NO: 1. No structure or function is provided for these functional equivalents have been set forth; therefore, the specification lacks written description of these equivalents.

Claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Notchless is an intracellular

polypeptide; therefore it is not clear how one skilled in the art can make or use notchless as a therapeutic or diagnostic agent.

In *Ex parte Forman* (230 USPQ 546) the Board considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation:

1) Quantity of experimentation necessary: To determine intracellular proteins as therapeutic or diagnostic agents, or uses there in, would require undue experimentation because intracellular proteins that modulate early embryonic receptor activity such as Notch, are expressed intracellularly, not administered extracellularly.

2) Amount of direction or guidance presented: No guidance is provided.

3) Presence or absence of working examples: No working examples are provided.

4) Nature of the invention; 5) State of the prior art; 6) Relative skill of those in the art: The invention is complex and the prior art does not recognize the administration of intracellular early embryonic proteins are uses as pharmaceuticals or diagnostics. Those working in this art are highly skilled.

7) Predictability or unpredictability of the art: Without any prior art or showing in the instant invention, it is not predictable that Notchless could be used as a therapeutic or diagnostic agent.

8) Breadth of the claims: The claims are broad and drawn not only to Notchless but also to undescribed equivalents.

For all of these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.. It is not clear what the function of a functional equivelent of SEQ ID NO: 1 is.

In Claims 2 and 3, it is not clear how the protein or fragment thereof regulates activity of Notch gene family products.

In Claim 5, "claim" should be --- claims ---. Claim 5 broadens Claim 1-4 because the protein or fragment of the protein must comprise SEQ ID NO: 1. Also, mutations are by deletion, insertion, or substitution; thus, it is not clear what is further meant by the term mutation in Claim 5.

In Claim 6, DNA is recombinant, protein is not. Therefore, "recombinant" should be changed to --- recombinantly produced --, for example.

In Claim 7, it is not clear what "binds specifically" means, when by definition the binding cannot be specific if it binds to any Notch gene product.

It is not clear in Claims 8 and 9 how the protein or fragment thereof can be associated with an enzyme or reporter. What is considered to be a reporter?

In Claims 13 and 14, it is not clear what therapy or pharmaceutical application the protein will be used in.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 5-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Royet et al. (December 15, 1998; EMBO J. 17(24): 7351-7360). Royet et al. teach *Drosophila* Notchless, a functional equivalent of SEQ ID NO: 1 having a Gln at amino acid residue 283 instead of a His (Claim 1). Notchless regulates the activityof a protein product of Notch gene family (Claim 2) by increasing Notch 1 activity (page 7356; Claim 3). The Notchless was recombinantly produced (page 7353; Claim 6). Notchless binds to the intracellular domain of Notch (page 7357, left col) and increases Notch activity which is activated by cleaves of the intracellular domain (Claim 8, 9). Hemaglutinin (HA was fused to Notchless (page 7359, left col.; Claim 10). Notchless was labeled with ^{35}S (page 7359, left col. "GST-Fusion protein binding assay"; Claim 11).

Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Rubin et al. (USP 6, 319,704, priority to August 29, 1996). Rubin et al. teach KUZ, that regulates Notch signalling by proteolytically cleaving the intracellular domain of Notch and therefore activating Notch (col. 17, lines 61-63). Thus KUZ is a functional equivalent of Notchless in that it activates Notch (Claims 1-3). KUZ was derived from *Drosophila*, human, and mouse (Example 2; Claim 4). KUZ was truncated and therefore altered by deletion insertion, substutition (col. 14, line 62; Claim 5) and expressed via cloning (Example 2), thus recombinantly produced (Claim 6). KUZ is associated with an exzyme because it is a enzyme (protease; Claims 8, 9) and binds to the intracellular domain of Notch (Claim 7).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 703-308-0034. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 703-308-2329. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

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KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER